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Commentary: The Goldilocks principle—selective antegrade cerebral perfusion optimizes cerebral tissue oxygenation

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Adverse neurologic outcomes remain a prominent cause of morbidity after repair of complex congenital heart disease (CHD)¹ and continue to remain a thorn in the side of congenital heart surgeons. Although adverse outcomes are multifactorial, often related to nonmodifiable patient factors, cerebral protection during cardiopulmonary bypass (CPB) is an important modifiable factor influencing postoperative neurologic function. Further insight into the link between altered cerebral perfusion and cerebral injury is critical to improve long-term outcomes for children with CHD.

In the current issue of the *Journal*, Mavroudis and colleagues² report their results comparing cerebral perfusion strategies using a neonatal swine model. Specifically, they compared selective antegrade cerebral perfusion (SACP) with deep hypothermic circulatory arrest (DHCA) and continuous deep hypothermic CPB (DHCPB). Study animals were cooled to 18°C for 40 minutes and normothermic CPB and sham animals were used as control groups. Intraoperative cerebral blood flow (CBF) was directly measured, and noninvasive cerebral spectroscopy was used to monitor markers of cerebral oxygenation and oxygen extraction. Subsequently, animals were killed, and cerebral tissue was evaluated to assess mitochondrial function and production of reactive oxygen species (ROS) generation. Respiratory control ratio (RCR), in effect, is the ratio of mitochondrial ATP production to mitochondrial permeability and

The Goldilocks principle.

CENTRAL MESSAGE

Matching oxygen supply to demand during cerebral perfusion limits cellular derangement and may be a strategy to alleviate adverse neurologic outcomes after neonatal congenital heart surgery.

represents a global marker of mitochondrial function (ie, greater RCR equals better mitochondrial function).³ Alternatively, excess ROS production is toxic to cellular proteins and is associated with secondary neuronal death after a stressful insult.⁴

The key findings indicated that SACP was associated with better matching of oxygen delivery to demand when compared with DHCA and continuous hypothermic CPB. That is, decreased CBF seen with DHCA resulted in poor tissue oxygenation and increased oxygen extraction. Indeed, this translated into increased cellular defragmentation, as evident by significantly worse mitochondrial function (ie, lower RCR levels) and increased ROS generation. Conversely, the DHCPB group demonstrated increased ROS generation compared with SACP. Interestingly, the DHCPB group did not demonstrate increased mitochondrial dysfunction, suggesting that increased oxygen delivery resulted in ROS generation without tissue injury.

By pairing results of intraoperative cerebral oxygenation with histologic cerebral tissue samples, this study provides an important link between how operative management of altered CBF influences cerebral cellular function. Although the findings are somewhat intuitive, that is, the results follow the “Goldilocks” principle that either too much or too little can be detrimental (Figure 1), concrete evidence corroborating this link is not easily demonstrated in congenital heart surgery. As the authors point out, conclusive evidence demonstrating superiority among cerebral-protection

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Disclosures: The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Jan 6, 2021; revisions received Jan 6, 2021; accepted for publication Jan 8, 2021; available ahead of print Jan 20, 2021.

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J Thorac Cardiovasc Surg 2022;163:e61-2

0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2021.01.025>

FIGURE 1. The Goldilocks principle.

strategies has not clearly been identified—in part because of the large variations in institutional practice of SACP implementation. In adults undergoing cardiac surgery, a compelling case can be made that ACP provides significantly better cerebral protection compared with DHCA.⁵ However, direct extrapolation of these results to the pediatric population is limited, given the discrepancy in neuronal development between adults and neonates.⁶

Despite excellent survival, impaired early- and long-term neurologic impairment remains an Achilles' heel within congenital heart surgery. While the results of the current study are not directly clinically translatable, they do provide an important clinical message—matching cerebral perfusion to metabolic demand is critical to enhance neurologic outcomes among neonates with CHD. Mavroudis and colleagues have provided a study that will help optimize

cerebral-protection strategies and ultimately may lead to better outcomes.

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